EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1180	(544/331).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/03/04 10:52
L2	1738	(544/405).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/03/04 10:52
L3	701	(514/255.01).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/03/04 10:52

EAST Search History

L4	2688	(514/365).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/03/04 10:52
L5	894	(548/146).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2007/03/04 10:52
L6	1	L1 AND L3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/03/04 10:54

EAST Search History

L7	166	L2 AND L1	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/03/04 10:53
L8	13	L7 AND L4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/03/04 10:53

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

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NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 26	FEB 13	CASREACT coverage to be extended
NEWS 27	Feb 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 28	Feb 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 29	Feb 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 30	Feb 26	MEDLINE reloaded with enhancements
NEWS 31	Feb 26	EMBASE enhanced with Clinical Trial Number field
NEWS 32	Feb 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 33	Feb 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 34	Feb 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT

SAEED

MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 10:01:16 ON 04 MAR 2007

=> FILE REG

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.42

FILE 'REGISTRY' ENTERED AT 10:02:05 ON 04 MAR 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 MAR 2007 HIGHEST RN 924584-96-3
DICTIONARY FILE UPDATES: 2 MAR 2007 HIGHEST RN 924584-96-3

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

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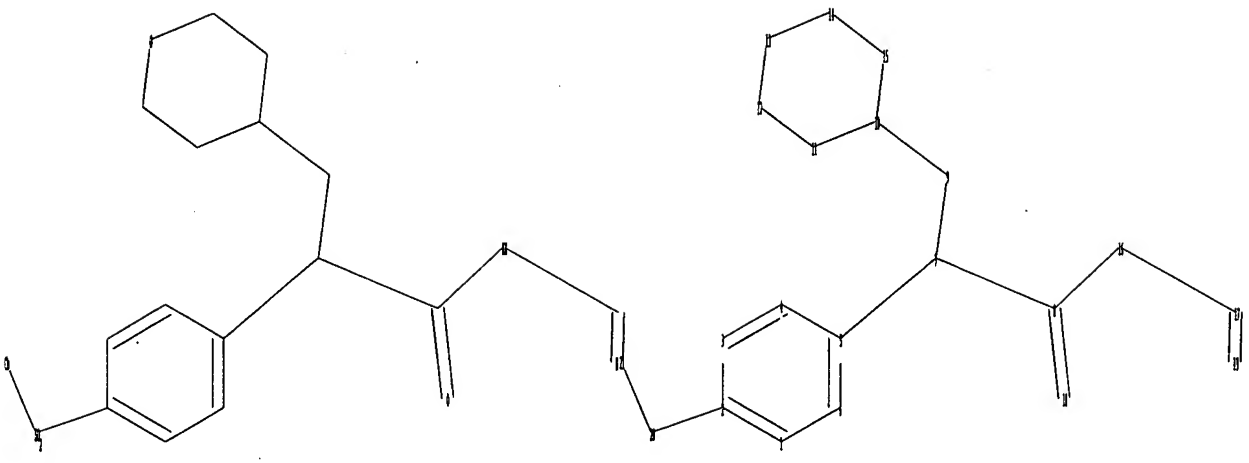

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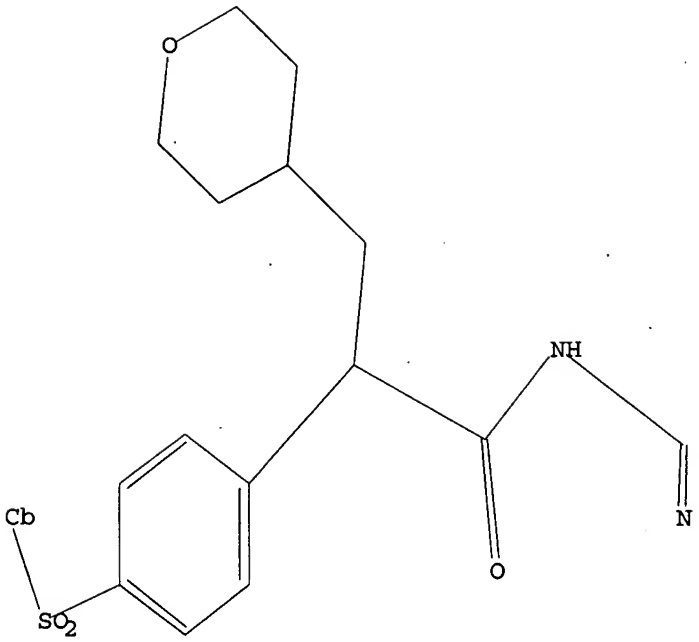
7 8 9 16 17 18 20 21
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 19
chain bonds :
2-20 5-7 7-8 7-9 8-16 8-18 9-10 16-17 17-19 20-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15
exact/norm bonds :
8-16 8-18 16-17 17-19
exact bonds :
2-20 5-7 7-8 7-9 9-10 10-11 10-15 11-12 12-13 13-14 14-15 20-21
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 10 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:Atom
20:CLASS 21:Atom

L1 STRUCTURE UPLOADED

=> D
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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100.0% PROCESSED         0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:             0 TO        0
PROJECTED ANSWERS:                0 TO        0

L2             0 SEA SSS SAM L1

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Uploading C:\Program Files\Stnexp\Queries\107765841.str
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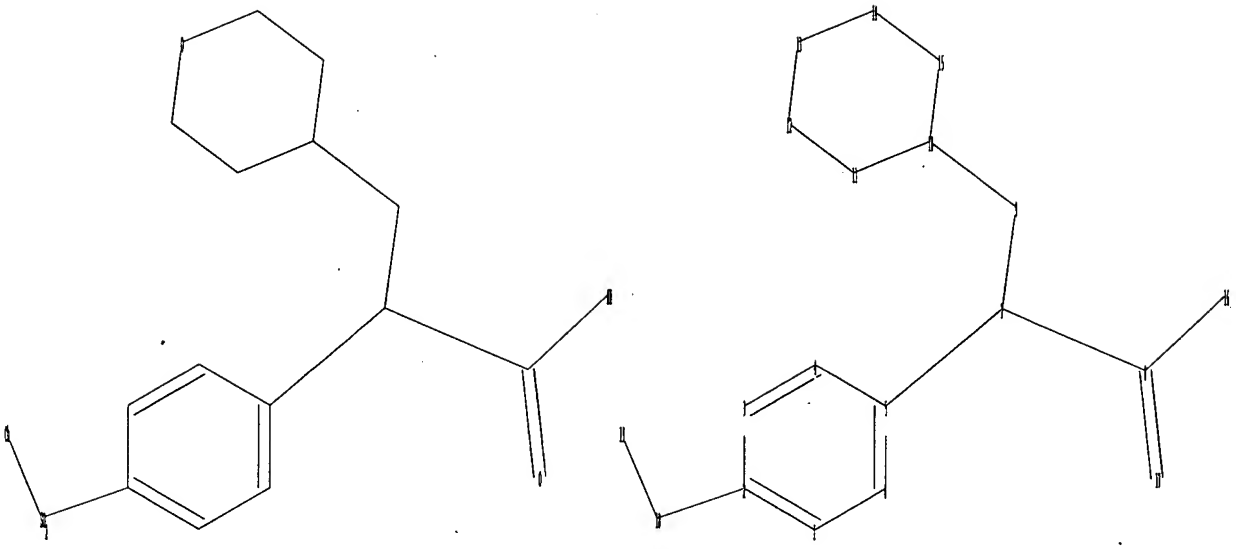

chain nodes :
7 8 9 16 17 18 19
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15
chain bonds :
2-18 5-7 7-8 7-9 8-16 8-17 9-10 18-19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15
exact/norm bonds :
8-16 8-17
exact bonds :
2-18 5-7 7-8 7-9 9-10 10-11 10-15 11-12 12-13 13-14 14-15 18-19
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 10 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:Atom

L3 STRUCTURE UPLOADED

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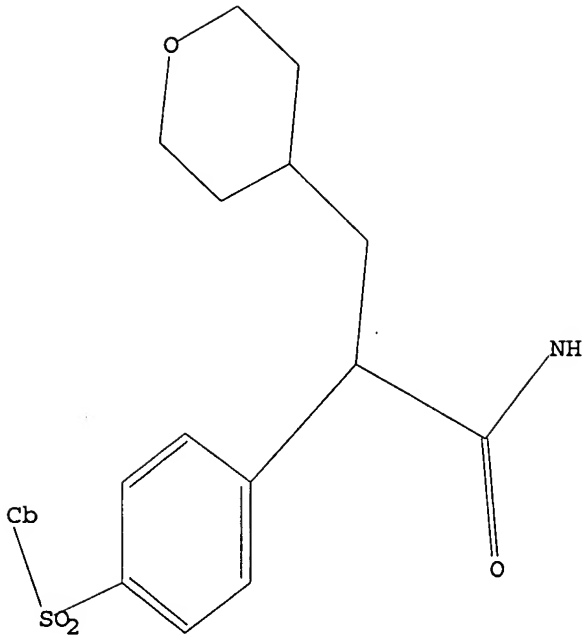
L3 HAS NO ANSWERS
L3 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -       13 TO ITERATE

100.0% PROCESSED       13 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           44 TO      476
PROJECTED ANSWERS:               1 TO       80

L4             1 SEA SSS SAM L3

=> S L3 FULL
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FULL SCREEN SEARCH COMPLETED -      178 TO ITERATE

100.0% PROCESSED      178 ITERATIONS                               19 ANSWERS
SEARCH TIME: 00.00.01

L5            19 SEA SSS FUL L3

=> FILE CAPLUS
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   173.45     173.87

FILE 'CAPLUS' ENTERED AT 10:04:14 ON 04 MAR 2007
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FILE COVERS 1907 - 4 Mar 2007 VOL 146 ISS 11
FILE LAST UPDATED: 2 Mar 2007 (20070302/ED)

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=> S L5
L6 3 L5

=> D IBIB ABS HITSTR TOT

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:152758 CAPLUS
DOCUMENT NUMBER: 144:232918
TITLE: Enantioselective hydrogenation process using ruthenium or rhodium with Mandyphos ligand in alcohols for production of 2-substituted propanoic acid derivatives, and their pharmaceutical compositions, and use for prophylactic or therapeutic treatment of conditions activated by glucokinase
INVENTOR(S): Briner, Paul Howard; Fyfe, Matthew Colin Thor; Madeley, John Paul; Murray, Peter John; Procter, Martin James; Spindler, Felix
PATENT ASSIGNEE(S): Prosidion Limited, UK
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006016178	A1	20060216	WO 2005-GB3175	20050812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

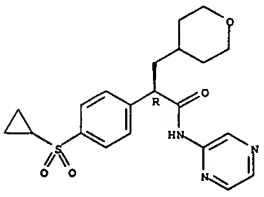
PRIORITY APPLN. INFO.: GB 2004-18046 A 20040812

OTHER SOURCE(S): CASREACT 144:232918; MARPAT 144:232918
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

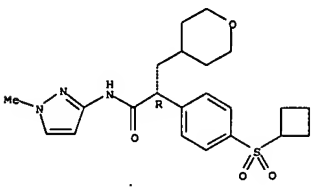
AB A process is disclosed for the production of pharmaceutical intermediates I, comprising the enantioselective hydrogenation of 2-substituted acrylic acid derivs. The acid chlorides of compds. I, wherein R is cyclopropyl or cyclobutyl, are also claimed. I were produced via asym. hydrogenation of acrylic acids II using either rhodium or ruthenium catalysts in the presence of (R)-(S)-MOD-Mandyphos ligands and using alcs. as solvents. Example compound III was prepared by Friedel-Crafts acylation of cyclopropyl

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 745051-73-4 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclobutylsulfonyl)phenyl]tetrahydro-N-(1-methyl-1H-pyrazol-3-yl)-, (αR)- (9CI) (CA INDEX NAME)

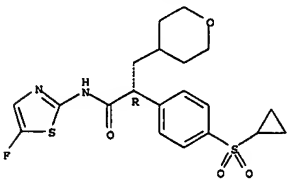
Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Ph sulfide with Et chlorooxoacetate, and the resulting Et [4-(cyclopropylsulfanyl)phenyl]oxoacetate was oxidized to the corresponding sulfonyl compd., which underwent olefination with triphenyl[(tetrahydropyran-4-yl)methyl]phosphonium iodide, and the resulting substituted acrylic acid underwent asym. hydrogenation to give compd. III. The invention also provides a method of prophylaxis or treatment of conditions activated by glucokinase (no data) using derived pharmaceuticals, e.g., IV, which are prepd. from I.
IT 745051-61-0P, (2R)-2-(4-(Cyclopropylsulfonyl)phenyl)-N-(5-fluorothiazol-2-yl)-3-(tetrahydropyran-4-yl)propionamide 745051-65-4P, (2R)-2-(4-(Cyclopropylsulfonyl)phenyl)-N-(pyrazin-2-yl)-3-(tetrahydropyran-4-yl)propionamide 745051-73-4P, (2R)-2-(4-(Cyclobutylsulfonyl)phenyl)-N-(1-methyl-1H-pyrazol-3-yl)-3-(tetrahydropyran-4-yl)propionamide
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; enantioselective hydrogenation using ruthenium or rhodium with Mandyphos ligand in alcs. for production of substituted propanoic acid derivs. used for treatment of glucokinase-mediated diseases)
RN 745051-61-0 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]-N-(5-fluoro-2-thiazolyl)tetrahydro-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 745051-65-4 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-N-pyrazinyl-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:151139 CAPLUS
DOCUMENT NUMBER: 144:233065
TITLE: Process for preparation of fluorinated thiazoles by fluorination of protected aminothiazole, and their use as intermediates in the synthesis of glucokinase activators
INVENTOR(S): Fyfe, Matthew Colin Thor; Naud, Frederic
PATENT ASSIGNEE(S): Prosidion Limited, UK
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006016174	A1	20060216	WO 2005-GB3170	20050812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: GB 2004-18058 A 20040812

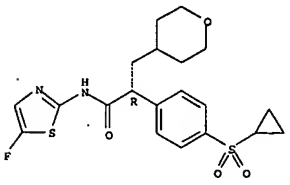
OTHER SOURCE(S): MARPAT 144:233065
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to a process for production of thiazole I or an acid addition salt thereof, by fluorination of a protected aminothiazole II [Pg = protecting group selected from acetyl, pivaloyl, tert-butoxycarbonyl (Boc)], followed by removal of the protecting group and optional salt formation. The invention is also related to the use of thiazoles I in the preparation of activators of glucokinase III [Q = aryl, 5- to 6-membered heteroaryl, 4- to 8-membered heterocyclyl; R1, R2 = independently H, CN, NO2, OMe, etc.; R5, R6 = independently H, halo, CN, SO2R8, SO2NH2 and derivs.; R8 = (un)substituted alk(en/yn)yl, cycloalkyl, etc.; X = (CH2)m; m = 0-1], and their pharmaceutically acceptable salts, for use in the treatment of hyperglycemia and type II diabetes. Thus, fluorination of 2-(tert-butoxycarbonylamino)thiazole with N-fluorobenzenesulfonimide in the presence of tert-Bu lithium/THF/pentane, followed by Boc-deprotection and acidulation with HCl gave (5-fluorothiazol-2-yl)amine•xHCl (IV). Coupling of (2R)-2-[4-(cyclopropylsulfonyl)phenyl]-3-(tetrahydropyran-4-

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
yl)propionic acid (prepn. given) with aminothiazole IV gave fluorinated amide V.
IT 745051-61-0P, (2R)-2-[4-(Cyclopropylsulfonyl)phenyl]-N-(5-fluorothiazol-2-yl)-3-(tetrahydropyran-4-yl)propionamide
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fluorinated thiazoles by fluorination of protected aminothiazole, and their use as intermediates in the synthesis of glucokinase activators)
RN 745051-61-0 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]-N-(5-fluoro-2-thiazolyl)tetrahydro-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:696344 CAPLUS
DOCUMENT NUMBER: 141:225496
TITLE: Preparation of tri(cyclo) substituted amides, in particular N-(thiazol-2-yl) amides, as Glucokinase (GK) activators for treating hyperglycemia and diabetes
INVENTOR(S): Fyfe, Matthew Colin Thor; Gardner, Lisa Sarah; Nawano, Masao; Procter, Martin James; Rasamison, Chrystelle Marie; Schofield, Karen Lesley; Shah, Vilasben Kanji; Yasuda, Kosuke
PATENT ASSIGNEE(S): Osi Pharmaceuticals, Inc., USA; Prosidion Ltd; Osi Pharm Inc
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004072031	A2	20040826	WO 2004-US3968	20040203
WO 2004072031	A3	20041202		
WO 2004072031	A8	20051006		
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AU 2004212500	A1	20040826	AU 2004-212500	20040203
CA 2515670	A1	20040826	CA 2004-2515670	20040203
CN 1809561	A	20060726	CN 2004-80009651	20040203
US 2004181067	A1	20040916	US 2004-776584	20040210
EP 1594867	A2	20051116	EP 2004-707845	20040210
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BR 2004007139	A	20060207	BR 2004-7139	20040210
JP 2006517590	T	20060727	JP 2006-503482	20040210
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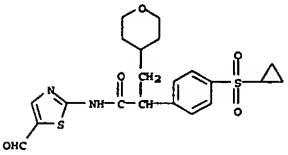
PRIORITY APPLN. INFO.: US 2003-446683P P 20030211
US 2003-494434P P 20030811
US 2003-512800P P 20031020
WO 2004-US3968 A 20040203

OTHER SOURCE(S): MARPAT 141:225496
GI

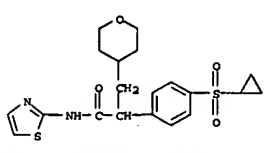
L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein Q = aryl, 5- or 6-membered heteroaryl, 4-8 membered heterocyclyl; T-N:C = monounsatd. heteroaryl, heterocyclyl; R1, R2 = independently H, OH, halo, CN, NO2, vinyl, ethynyl, methoxy, CHO, etc.; or R1R2 = carbocyclyl or heterocyclyl; or R1R2 = :O; R3, R4 = independently H, halo, mrthoxy, CO2H and derivs., CN, NO2, CHO, CONH2 and derivs., (un)substittued aryl, heteroaryl, cycloalkyl, etc.; or R3R4 = 5-8 membered hetero/aromatic, carbocylic or heterocylic ring; R5, R6 = independently H, OH, halo, CN, NO2, CO2H and derive., CHO, C(:NOH)H and derivs., S(O)pH and derivs., NH2 and derivs., (un)substituted alk(en/yn)yl, hetero/aryl, etc.; p = 0-2; X = (CH2)m; m = 0-1; the dotted line together with the solid line = optionally double bond with (E)-configuration; and ther pharmaceutically acceptable salts] were prepared as Glukokinase (GK) activators. For example, II was prepared, in 2 steps, by condensation of 3-thiophenecarboxaldehyde with [4-(Methanesulfonyl)phenyl]acetic acid in toluene in the presence of piperidine, and coupling of the resulting acrylic acid with 2-thiazolamine. Preferred I produced EC50s ranging from 0.1 to 32.6 μM with max FAs from 1.6 to 8.7 in vitro, demonstrating their GK activator activity. Thus, I are useful for treating hyperglycemia and diabetes (no data).
IT 745051-53-0P, 2-[4-(Cyclopropylsulfonyl)phenyl]-N-(5-formylthiazol-2-yl)-3-(tetrahydropyran-4-yl)propionamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(GK activator; preparation of tri(cyclo) substituted amides, in particular N-thiazolyl amides, as Glucokinase (GK) activators for treating hyperglycemia and diabetes)
RN 745051-53-0 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]-N-(5-formyl-2-thiazolyl)tetrahydro- (9CI) (CA INDEX NAME)

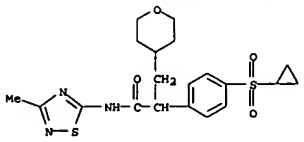


IT 745050-76-4P, 2-[4-(Cyclopropylsulfonyl)phenyl]-3-(tetrahydropyran-4-yl)-N-(thiazol-2-yl)propionamide 745050-98-0P, 2-[4-(Cyclopropylsulfonyl)phenyl]-N-(3-methyl-[1,2,4]thiadiazol-5-yl)-3-(tetrahydropyran-4-yl)propionamide 745050-99-1P, 2-[4-(Cyclopropylsulfonyl)phenyl]-N-pyrazin-2-yl-3-(tetrahydropyran-4-yl)propionamide 745051-00-7P, 2-[4-(Cyclopropylsulfonyl)phenyl]-3-(tetrahydropyran-4-yl)-N-[1,2,4]thiadiazol-5-ylpropionamide 745051-61-0P, (2R)-2-[4-(Cyclopropylsulfonyl)phenyl]-N-(5-fluorothiazol-2-yl)-3-(tetrahydropyran-4-yl)propionamide 745051-64-3P, (2R)-2-[4-(Cyclopropylsulfonyl)phenyl]-3-(tetrahydropyran-4-yl)-N-[1,2,4]thiadiazol-5-ylpropionamide 745051-65-4P, (2R)-2-[4-(Cyclopropylsulfonyl)phenyl]-N-pyrazin-2-yl-3-(tetrahydropyran-4-yl)propionamide 745051-67-6P, (2R)-2-[4-(Cyclopropylsulfonyl)phenyl]-N-(5-fluoropyridin-2-yl)-3-(tetrahydropyran-4-yl)propionamide 745051-68-7P, (2R)-2-[4-(Cyclopropylsulfonyl)phenyl]-3-(tetrahydropyran-4-yl)-N-(thiazol-2-yl)propionamide 745051-69-8P, (2R)-2-[4-(Cyclopropylsulfonyl)phenyl]-N-(3-methyl-[1,2,4]thiadiazol-5-yl)-3-(tetrahydropyran-4-yl)propionamide 745051-70-1P, (2R)-2-[4-(Cyclobutylsulfonyl)phenyl]-N-pyrazin-2-yl-3-(tetrahydropyran-4-yl)propionamide 745051-71-2P, (2R)-2-[4-(Cyclobutylsulfonyl)phenyl]-N-pyrimidin-4-yl-3-(tetrahydropyran-4-yl)propionamide 745051-72-3P, (2R)-2-[4-(Cyclobutylsulfonyl)phenyl]-N-(isoxazol-3-yl)-3-(tetrahydropyran-4-yl)propionamide 745051-73-4P, (2R)-2-[4-(Cyclobutylsulfonyl)phenyl]-N-(1-methyl-1H-pyrazol-3-yl)-3-(tetrahydropyran-4-yl)propionamide 745051-74-5P, (2R)-2-[4-(Cyclobutylsulfonyl)phenyl]-N-(5-fluorothiazol-2-yl)-3-(tetrahydropyran-4-yl)propionamide 745052-00-0P, N-(5-Cyanothiazol-2-yl)-2-[4-(cyclopropylsulfonyl)phenyl]-3-(tetrahydropyran-4-yl)propionamide 745052-29-3P, 2-[4-(Cyclobutylsulfonyl)phenyl]-3-(tetrahydropyran-4-yl)-N-(thiazol-2-yl)propionamide 745052-69-1P, 2-[4-(Cyclopropylsulfonyl)phenyl]-N-(5-fluorothiazol-2-yl)-3-(tetrahydropyran-4-yl)propionamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GK activator; prepn. of tri(cyclo) substituted amides, in particular N-thiazolyl amides, as Glucokinase (GK) activators for treating hyperglycemia and diabetes)
RN 745050-76-4 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-N-2-thiazolyl- (9CI) (CA INDEX NAME)

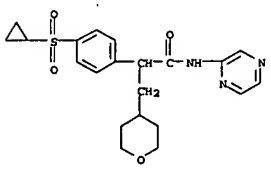


RN 745050-98-0 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-N-(3-methyl-1,2,4-thiadiazol-5-yl)- (9CI) (CA INDEX NAME)

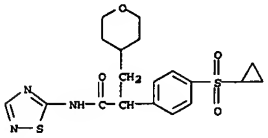
L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 745050-99-1 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-N-pyrazinyl- (9CI) (CA INDEX NAME)



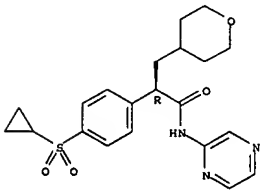
RN 745051-00-7 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-N-1,2,4-thiadiazol-5-yl- (9CI) (CA INDEX NAME)



RN 745051-61-0 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]-N-(5-fluoro-2-thiazolyl)tetrahydro-, (αR)- (9CI) (CA INDEX NAME)

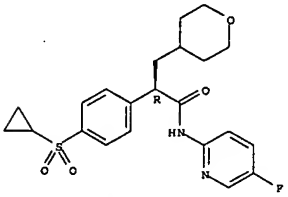
Absolute stereochemistry.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



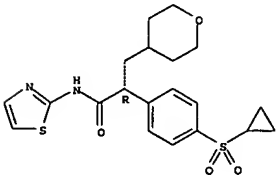
RN 745051-67-6 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]-N-(5-fluoro-2-pyridinyl)tetrahydro-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

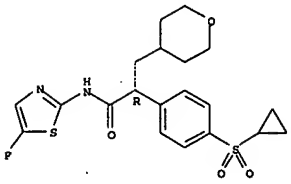


RN 745051-68-7 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-N-2-thiazolyl-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

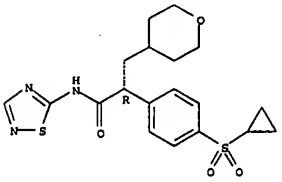


L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 745051-64-3 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-N-1,2,4-thiadiazol-5-yl-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



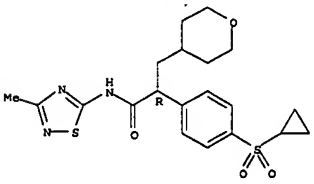
RN 745051-65-4 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-N-pyrazinyl-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

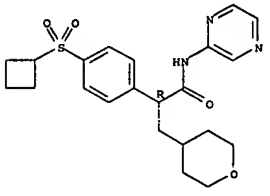
RN 745051-69-8 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-N-(3-methyl-1,2,4-thiadiazol-5-yl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 745051-70-1 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclobutylsulfonyl)phenyl]tetrahydro-N-pyrazinyl-, (αR)- (9CI) (CA INDEX NAME)

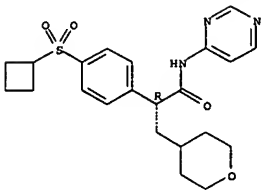
Absolute stereochemistry.



RN 745051-71-2 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclobutylsulfonyl)phenyl]tetrahydro-N-4-pyrimidinyl-, (αR)- (9CI) (CA INDEX NAME)

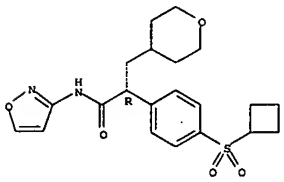
Absolute stereochemistry.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 745051-72-3 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclobutylsulfonyl)phenyl]tetrahydro-N-3-isoxazolyl-, (αR)- (9CI) (CA INDEX NAME)

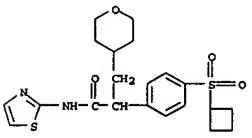
Absolute stereochemistry.



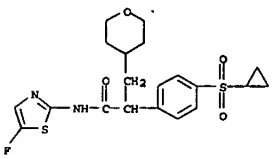
RN 745051-73-4 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclobutylsulfonyl)phenyl]tetrahydro-N-(1-methyl-1H-pyrazol-3-yl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

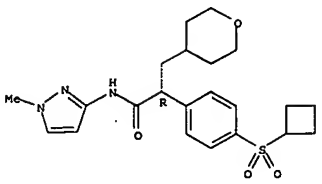


RN 745052-29-3 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclobutylsulfonyl)phenyl]tetrahydro-N-2-thiazolyl- (9CI) (CA INDEX NAME)



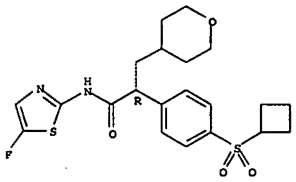
RN 745052-69-1 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclopropylsulfonyl)phenyl]-N-(5-fluoro-2-thiazolyl)tetrahydro- (9CI) (CA INDEX NAME)

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

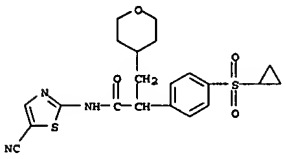


RN 745051-74-5 CAPLUS
CN 2H-Pyran-4-propanamide, α-[4-(cyclobutylsulfonyl)phenyl]-N-(5-fluoro-2-thiazolyl)tetrahydro-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 745052-00-0 CAPLUS
CN 2H-Pyran-4-propanamide, N-(5-cyano-2-thiazolyl)-α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro- (9CI) (CA INDEX NAME)



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ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:Y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   16.28     190.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -2.34      -2.34

STN INTERNATIONAL LOGOFF AT 10:04:48 ON 04 MAR 2007
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MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 11:12:37 ON 04 MAR 2007

=> FILE REG

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 2 MAR 2007 HIGHEST RN 924584-96-3
DICTIONARY FILE UPDATES: 2 MAR 2007 HIGHEST RN 924584-96-3

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http://www.cas.org/ONLINE/UG/regprops.html

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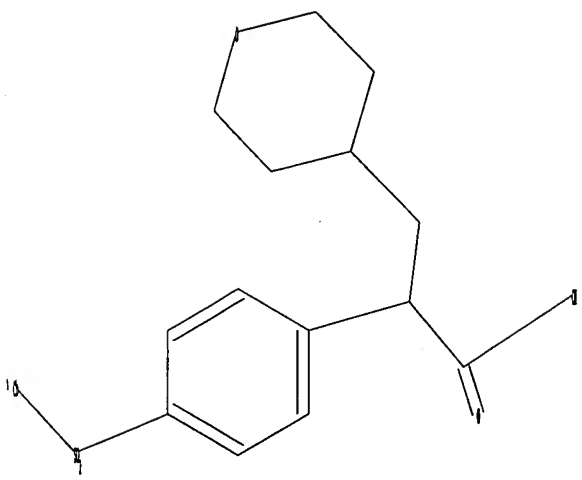
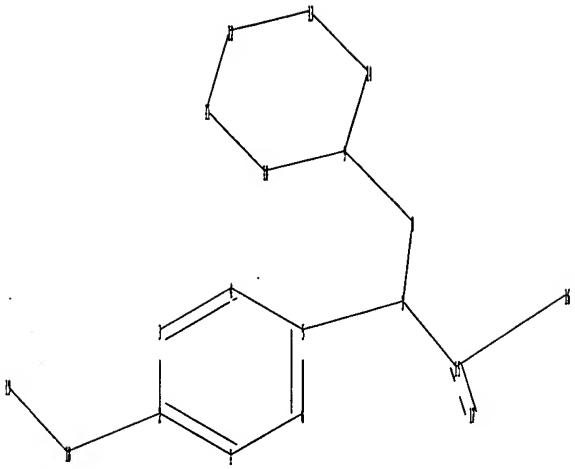
Uploading C:\Program Files\Stnexp\Queries\107765842.str





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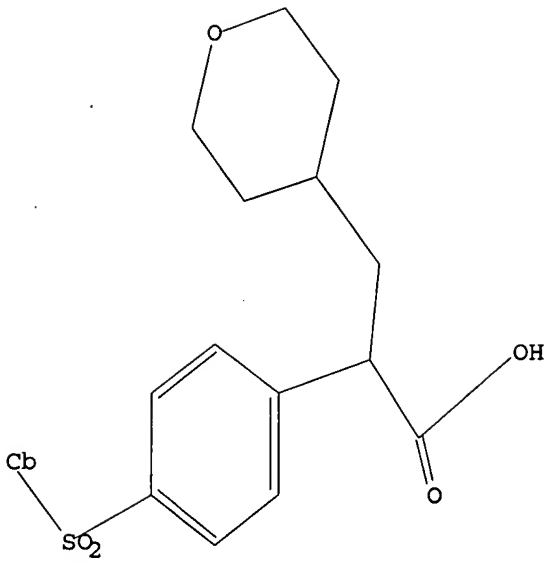
7 8 15 16 17 18 19
ring nodes :
1 2 3 4 5 6 9 10 11 12 13 14
chain bonds :
2-18 5-7 7-8 7-15 8-9 15-16 15-17 18-19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 9-10 9-14 10-11 11-12 12-13 13-14
exact bonds :
2-18 5-7 7-8 7-15 8-9 9-10 9-14 10-11 11-12 12-13 13-14 18-19
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-17
isolated ring systems :
containing 1 : 9 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:Atom

L1 STRUCTURE UPLOADED

=> D
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -      11 TO ITERATE

100.0% PROCESSED       11 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           22 TO      418
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> S L1 FULL
FULL SEARCH INITIATED 11:13:23 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      234 TO ITERATE

100.0% PROCESSED      234 ITERATIONS                                5 ANSWERS
SEARCH TIME: 00.00.01

L3            5 SEA SSS FUL L1

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                    172.10     172.31

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FILE LAST UPDATED: 2 Mar 2007 (20070302/ED)

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=> S L3
L4 3 L3

=> D IBIB ABS HITSTR TOT

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:152758 CAPLUS
DOCUMENT NUMBER: 144:232918
TITLE: Enantioselective hydrogenation process using ruthenium or rhodium with Mandyphos ligand in alcohols for production of 2-substituted propanoic acid derivatives, and their pharmaceutical compositions, and use for prophylactic or therapeutic treatment of conditions activated by glucokinase
INVENTOR(S): Briner, Paul Howard; Fyfe, Matthew Colin Thor; Madeley, John Paul; Murray, Peter John; Procter, Martin James; Spindler, Felix
PATENT ASSIGNEE(S): Prosidion Limited, UK
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006016178	A1	20060216	WO 2005-GB3175	20050812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: GB 2004-18046 A 20040812

OTHER SOURCE(S): CASREACT 144:232918; MARPAT 144:232918
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process is disclosed for the production of pharmaceutical intermediates I, comprising the enantioselective hydrogenation of 2-substituted acrylic acid derivs. The acid chlorides of compds. I, wherein R is cyclopropyl or cyclobutyl, are also claimed. I were produced via asym. hydrogenation of acrylic acids II using either rhodium or ruthenium catalysts in the presence of (R)-(S)-MOD-Mandyphos ligands and using alcs. as solvents. Example compound III was prepared by Friedel-Crafts acylation of cyclopropyl

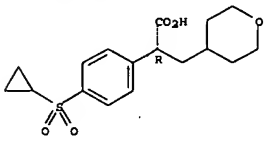
L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Ph sulfide with Et chlorooxoacetate, and the resulting Et [4-(cyclopropylsulfanyl)phenyl]oxoacetate was oxidized to the corresponding sulfonyl compd., which underwent olefination with triphenyl[(tetrahydropyran-4-yl)methyl]phosphonium iodide, and the resulting substituted acrylic acid underwent asym. hydrogenation to give compd. III. The invention also provides a method of prophylaxis or treatment of conditions activated by glucokinase (no data) using derived pharmaceuticals, e.g., IV, which are prepd. from I.

IT 745053-49-0P, (2R)-2-(4-(Cyclopropylsulfonyl)phenyl)-3-(tetrahydropyran-4-yl)propionic acid 745053-51-4P, (2R)-2-(4-(Cyclobutylsulfonyl)phenyl)-3-(tetrahydropyran-4-yl)propionic acid
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; enantioselective hydrogenation using ruthenium or rhodium with Mandyphos ligand in alcs. for production of substituted propanoic acid derivs. used for treatment of glucokinase-mediated diseases)

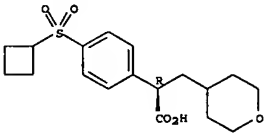
RN 745053-49-0 CAPLUS
CN 2H-Pyran-4-propanoic acid, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 745053-51-4 CAPLUS
CN 2H-Pyran-4-propanoic acid, α-[4-(cyclobutylsulfonyl)phenyl]tetrahydro-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:151139 CAPLUS
DOCUMENT NUMBER: 144:233065
TITLE: Process for preparation of fluorinated thiazoles by fluorination of protected aminothiazole, and their use as intermediates in the synthesis of glucokinase activators
INVENTOR(S): Fyfe, Matthew Colin Thor; Naud, Frederic
PATENT ASSIGNEE(S): Prosidion Limited, UK
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006016174	A1	20060216	WO 2005-GB3170	20050812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: GB 2004-18058 A 20040812

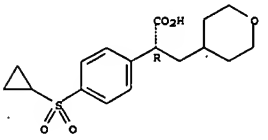
OTHER SOURCE(S): MARPAT 144:233065
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to a process for production of thiazole I or an acid addition salt thereof, by fluorination of a protected aminothiazole II [Pg = protecting group selected from acetyl, pivaloyl, tert-butoxycarbonyl (Boc)], followed by removal of the protecting group and optional salt formation. The invention is also related to the use of thiazoles I in the preparation of activators of glucokinase III (Q = aryl, 5- to 6-membered heteroaryl, 4- to 8-membered heterocyclyl; R1, R2 = independently H, CN, NO2, OMe, etc.; R5, R6 = independently H, halo, CN, SO2R8, SO2NH2 and derivs.; R8 = (un)substituted alk(en/yn)yl, cycloalkyl, etc.; X = (CH2)m; m = 0-1], and their pharmaceutically acceptable salts, for use in the treatment of hyperglycemia and type II diabetes. Thus, fluorination of 2-(tert-butoxycarbonylamino)thiazole with N-fluorobenzenesulfonimide in the presence of tert-Bu lithium/THF/pentane, followed by Boc-deprotection and acidulation with HCl gave (5-fluorothiazol-2-yl)amine•xHCl (IV). Coupling of (2R)-2-[4-(cyclopropylsulfonyl)phenyl]-3-(tetrahydropyran-4-

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
yl)propionic acid (prepn. given) with aminothiazole IV gave fluorinated amide V.
IT 745053-49-0P, (2R)-2-[4-(Cyclopropylsulfonyl)phenyl]-3-(tetrahydropyran-4-yl)propionic acid
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of fluorinated thiazoles by fluorination of protected aminothiazole, and their use as intermediates in the synthesis of glucokinase activators)
RN 745053-49-0 CAPLUS
CN 2H-Pyran-4-propanoic acid, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:696344 CAPLUS
DOCUMENT NUMBER: 141:225496
TITLE: Preparation of tri(cyclo) substituted amides, in particular N-(thiazol-2-yl) amides, as Glucokinase (GK) activators for treating hyperglycemia and diabetes
INVENTOR(S): Fyfe, Matthew Colin Thor; Gardner, Lisa Sarah; Nawano, Masao; Procter, Martin James; Rasamison, Chrystelle Marie; Schofield, Karen Lesley; Shah, Vilasben Kanji; Yasuda, Kosuke
PATENT ASSIGNEE(S): Osi Pharmaceuticals, Inc., USA; Prosidion Ltd; Osi Pharm Inc
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004072031	A2	20040826	WO 2004-US3968	20040203
WO 2004072031	A3	20041202		
WO 2004072031	A8	20051006		
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004212500	A1	20040826	AU 2004-212500	20040203
CA 2515670	A1	20040826	CA 2004-2515670	20040203
CN 1809561	A	20060726	CN 2004-80009651	20040203
US 2004181067	A1	20040916	US 2004-776584	20040210
EP 1594867	A2	20051116	EP 2004-707845	20040210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007139	A	20060207	BR 2004-7139	20040210
JP 2006517590	T	20060727	JP 2006-503482	20040210
IN 2005MN00840	A	20051202	IN 2005-MN840	20050802
NO 2005003742	A	20050829	NO 2005-3742	20050804

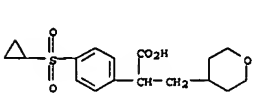
PRIORITY APPLN. INFO.: US 2003-446683P P 20030211
US 2003-494434P P 20030811
US 2003-512800P P 20031020
WO 2004-US3968 A 20040203

OTHER SOURCE(S): MARPAT 141:225496
GI

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

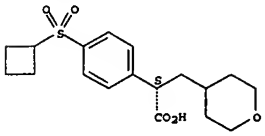
AB Title compds. I [wherein Q = aryl, 5- or 6-membered heteroaryl, 4-8 membered heterocyclyl; T-N:C = monounsatd. heteroaryl, heterocyclyl; R1, R2 = independently H, OH, halo, CN, NO2, vinyl, ethynyl, methoxy, CHO, etc.; or R1R2 = carbocyclyl or heterocyclyl; or R1R2 = :O; R3, R4 = independently H, halo, mrthoxy, CO2H and derivs., CN, NO2, CHO, CONH2 and derivs., (un)substittued aryl, heteroaryl, cycloalkyl, etc.; or R3R4 = 5-8 membered hetero/aromatic, carbocylic or heterocylic ring; R5, R6 = independently H, OH, halo, CN, NO2, CO2H and derivs., CHO, C(:NOH)H and derivs., S(O)pH and derivs., NH2 and derivs., (un)substituted alk(en/yn)yl, hetero/aryl, etc.; p = 0-2; X = (CH2)m; m = 0-1; the dotted line together with the solid line = optionally double bond with (E)-configuration; and ther pharmaceutically acceptable salts] were prepared as Glukokinase (GK) activators. For example, II was prepared, in 2 steps, by condensation of 3-thiophenecarboxaldehyde with [4-(Methanesulfonyl)phenyl]acetic acid in toluene in the presence of piperidine, and coupling of the resulting acrylic acid with 2-thiazolamine. Preferred I produced EC50s ranging from 0.1 to 32.6 μM with max FAs from 1.6 to 8.7 in vitro, demonstrating their GK activator activity. Thus, I are useful for treating hyperglycemia and diabetes (no data).
IT 745052-93-1P, 2-[4-(Cyclopropylsulfonyl)phenyl]-3-(tetrahydropyran-4-yl)propionic acid 745053-25-2P 745053-41-2P, 2-[4-(Cyclobutylsulfonyl)phenyl]-3-(tetrahydropyran-4-yl)propionic acid 745053-49-0P 745053-51-4P, (2R)-2-[4-(Cyclobutylsulfonyl)phenyl]-3-(tetrahydropyran-4-yl)propionic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of tri(cyclo) substituted amides, in particular N-thiazolyl amides, as Glucokinase (GK) activators for treating hyperglycemia and diabetes)
RN 745052-93-1 CAPLUS
CN 2H-Pyran-4-propanoic acid, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro- (9CI) (CA INDEX NAME)



RN 745053-25-2 CAPLUS
CN 2H-Pyran-4-propanoic acid, α-[4-(cyclobutylsulfonyl)phenyl]tetrahydro-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 745053-41-2 CAPLUS
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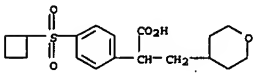
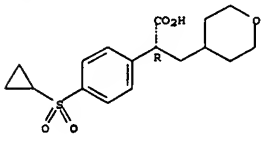


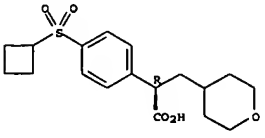
RN 745053-49-0 CAPLUS
CN 2H-Pyran-4-propanoic acid, α-[4-(cyclopropylsulfonyl)phenyl]tetrahydro-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 745053-51-4 CAPLUS
CN 2H-Pyran-4-propanoic acid, α-[4-(cyclobutylsulfonyl)phenyl]tetrahydro-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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